PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference L0461.70154	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US03/41189	International filing date *(day/month/year)* 22 December 2003 (22.12.2003)	Priority date *(day/month/year)* 22 December 2003 (22.12.2003)

International Patent Classification (IPC) or national classification and IPC

IPC: **C12Q 1/68**(2006.01);**A01N 43/04**(2006.01);**C07H 21/04**(2006.01);**A61K 31/07**(2006.01)
USPC: 424/134.1;435/6,91.1,325,375;536/23.1,24.3,24.33,24.5;514/44

Applicant

LUDWIG INSTITUTE FOR CANCER RESEARCH

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of ___ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
20 July 2005 (20.07.2005)	08 March 2006 (08.03.2006)
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/ US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Authorized officer Terra C. Gibbs Telephone No. (571) 272-1600

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US03/41189

I. Basis of the report

1. With regard to the elements of the international application:*

☒ the international application as originally filed.

☒ the description:
pages 1-42 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the claims:
pages 43-47, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the drawings:
pages 1-9, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the sequence listing part of the description:
pages 1-4, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☒ contained in the international application in printed form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages NONE

☐ the claims, Nos. NONE

☐ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*
*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US03/41189

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 2-6, 16-20, 33-37 and 46	YES
	Claims 1, 7-15, 21-32 and 38-54	NO
Inventive Step (IS)	Claims 2-6, 16-20, 33-37 and 46	YES
	Claims 1, 7-15, 21-32 and 38-54	NO
Industrial Applicability (IA)	Claims 1-54	YES
	Claims NONE	NO

2. CITATIONS AND EXPLANATIONS
Please See Continuation Sheet

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

V. 2. Citations and Explanations:
Claims 1-54 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

Claims 3-6, 17, 19, 20, 34, 36, 37, and 46 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest a method for inducing apoptosis in a cell comprising administering an siRNA that reduces the expression or activity of a mitotic checkpoint molecule, wherein the siRNA is BubR1, Bub3, or CENP-E.

Claims 1, 7-9, 11-15, 21-23, 25-32, 38-40, 42-45, 47-50, and 52-54 lack novelty under PCT Article 33(2) as being anticipated by Chan et al. Chan et al. disclose a method for inducing apoptosis in a cell comprising administering an antibody that reduces the expression or activity of a mitotic checkpoint molecule, wherein the antibody is BubR1 or Bub3 (see Figures 1-7).

Applicant's arguments filed December 14, 2005 have been fully considered and are found persuasive in part. In response to the holding of lack of novelty as being anticipated by Chan et al., Applicants traverse on the grounds that the Chan reference does not disclose that either anti-CENP-E antibodies or anti-hBURB1 antibodies alone increase apoptosis. Contrary to Applicant's traversal, the instant claims recite "comprising" language. The term "comprising" is open language. Therefore, the claims are broad and do not require that the anti-CENP-E antibodies or the anti-hBURB1 antibodies have to act alone in increasing apoptosis.

Applicants also argue that Chan et al. did not show, describe, or suggest any effect of anti-CENP-E antibodies or anti-hBURB1 antibodies on cancer or hyperprolifeartive disorder cells. This argument has been fully considered and is found persuasive. Chan do not describe or suggest any effect of anti-CENP-E antibodies or anti-hBURB1 antibodies on cancer or hyperprolifeartive disease in a subject.

Applicants also argue that Chan et al. does not describe the use of anti-Bub3 antibodies to increase apoptosis, but instead, only use anti-Bub3 antibodies for analyzing Bub3 expression on Western blots. This argument has been fully considered and is found persuasive as well. Chan only describe the use of anti-Bub3 antibodies for analyzing Bub3 expression on Western blots

Claims 1, 8, 10, 13, 15, 21, 22, 24, 27, 29-32, 38, 39, 41, 44, 47-49, 51, and 54 lack novelty under PCT Article 33(2) as

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

being anticipated by Gorbsky et al. Gorbsky et al. disclose a method for inducing apoptosis in a cell comprising administering an antibody that reduces the expression or activity of a mitotic checkpoint molecule, wherein the antibody is Mad2 (see Figures 1-11).

Applicants arguments filed December 14, 2005 have been fully considered and are found persuasive in part. In response to the holding of lack of novelty as being anticipated by Gorbsky et al., Applicants traverse on the grounds that first, the Gorbsky reference showed that microinjection of anti-Mad2 antibodies into two kinds of eukaryotic cells led to premature anaphase onset, but does not describe or suggest an effect of anti-Mad2 antibodies on apoptosis. Second, Applicants argue that the Gorbsky reference does not describe or suggest any effect of anti-Mad2 antibodies on cancer or a hyperproliferative disorder. Regarding Applicant's first traversal, although the Gorbsky reference does not describe or suggest an effect on anti-Mad2 antibodies on apoptosis, it is noted that this effect is inherent to the kangaroo kidney cells microinjected with the anti-Mad2 antibody. Therefore, absent evidence to the contrary, the kangaroo kidney cells microinjected with the anti-Mad2 antibody inherently increased apoptosis. Regarding Applicant's second traversal, the Examiner agrees that the Gorbsky reference does not describe or suggest any effect of anti-Mad2 antibodies on cancer or a hyperproliferative disorder.